REMARKS/ARGUMENTS

Summary of Status of Amendments

Initially, Applicants note with appreciation that the Examiner has allowed claims 14, 21-24, and 38.

In the present amendment, claims 15, 25-37, and 39 are amended, with claims 1-4, 8-9, 14-15, and 39 being independent claims. Claims 1-39 will remain pending with claims 15, 25-37, and 39 under consideration.

Applicants note that claims 15 and 25-36 have been amended to include the structural formulas of the compounds recited in the claims. Furthermore, claim 37 has been amended to remove the term "treated products such as" and "an immobilized products of cells or treated," and claim 39 has been amended as suggested by the Examiner to further clarify Applicants' invention. Applicants note that support for the amendment may be found throughout Applicants' originally filed disclosure.

Claim 15 has also been amended to recite the additional limitation that the claimed invention is an isolated DNA which "encodes for a polypeptide consisting of an amino acid sequence having about 99% homology with the amino acid sequence of SEQ ID NO: 1". Support for this amendment may be found in the specification as filed including at pages 9, 14-17, Example 5, and SEQ ID NOS: 1,2, 41, and 42. A person having ordinary skill in the art would understand, from reading the specification, that the claimed isolated DNA which codes for a polypeptide consisting of an amino acid sequence having about 99% homology with the amino acid sequence of SEQ ID NO: 1

is provided in the specification because the polynucleotide of SEQ ID NO: 41 which codes for a polypeptide consisting of the amino acid sequence of SEQ ID NO: 42 has a 99.7% homology with the amino acid sequence of SEQ ID NO: 1. Thus, one of ordinary skill in the art would understand that the specification provides adequate written description for the scope of amended claim 15 including an homology of "about 99%." No new matter has been added.

Reconsideration and withdrawal of the rejections and allowance of the application are respectfully requested.

Claim of Priority

Applicants express appreciation for the acknowledgement of the claim of priority to JP 11/21707 filed January 29, 1999, as well as receipt of the certified copy of the document.

Information Disclosure Statement

Applicants express appreciation for the consideration of the Information Disclosure Statement, filed December 28, 2001, by including an initialed copy of the Form PTO-1449 submitted therewith.

Restriction Requirement

Applicants note that the Examiner has maintained the restriction requirement

and made the requirement final with respect to claims 1-13 and 16-20, which remain withdrawn from consideration. However, Applicants respectfully request that claims 1-13 and 16-20 be permitted to remain pending subject to rejoinder should any of the pending claims be found to be allowable or upon allowance of the pending claims.

Response to Objection to Claim

Claim 39 is objected by the Examiner because it is partially directed to non-elected inventions, i.e., SEQ ID NO: 41, 43, and 44.

In response, Applicants have amended claim 39 to recite "(a) an oligonucleotide consisting of 5 to 60 continuous nucleotides of SEQ ID NO: 2, and (b) the complete complement of the oligonucleotide of (a)" as suggested by the Examiner.

Rejections under 35 U.S.C. § 112

Rejections for Indefiniteness

Claims 15, 25-37, and 39 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Applicants note that claims 15 and 25-36 are definite, but in order to advance prosecution of the present application, Applicants have made the following amendments.

Claims 15 and 25-36 are asserted to be indefinite because the recitation "I-a, I-b, II-a, II-b, III-a, III-b, IV-a, IV-b, VII-a, VII-b, VIII-a, VIII-b" do not clearly indicate which

compounds are being recited. The Examiner suggested amending the claims to recite either the commonly known chemical name of each of the compounds recited, or the structures corresponding to each of the compounds.

In response, Applicants have amended claims 15 and 25-36 to include the structural formulas corresponding to each of the compounds, as suggested by the Examiner.

Claim 15 is asserted to be indefinite because the recitation "DNA which hybridizes...under stringent conditions" is unclear which polynucleotide is claimed absent a statement of the conditions under which the hybridization reaction is performed.

In response, claim 15 has been amended to remove the recitation of the hybridization reaction.

Claims 29-36 are asserted to be indefinite because the recitation "the process according to claim...wherein the compound (X) is the compound (X) obtained by forming a lacton[e] from compound Y" or "the process according to claim...wherein the compound (X) is the compound (X) obtained by opening the lactone ring of compound Y" is unclear how the compound (X) is the same compound obtained after a modification. The Examiner suggested amending the term to read "the process according to claim...wherein the compound (X) is obtained by..." or "the process according to claim ...wherein the compound (X) is a compound obtained by..."

In response, Applicants have amended claims 29-36 as suggested by the

Examiner.

Claims 25-28 are asserted as being incomplete for omitting essential steps. The Examiner states that the claims are directed to a method for producing a compound X from a compound Y, however, a step is said to be missing wherein the enzyme responsible for the conversion is contacted with the reactant Y.

In response, claim 25 has been amended to include the recitation "in the presence of the enzyme source."

Claims 25-28 are rejected as being indefinite because the recitation "treated product of the culture" is unclear as to the meaning of the term within the context of the claim, and the specification provides no description of the term. The rejection asserts that the term "treated" is vague in regard to what has been done on the "product of the culture." In response, Applicants note that one of ordinary skill in the art would understand from reading the specification, especially at page 14, lines 1-6, and the examples of treated products of the culture described at page 27, lines 19-23, that the term "treated" in regard to the "product of the culture" means treated products of the culture of the cells.

Claim 37 is asserted to be indefinite because the recitation "the product of the culture of the transformant is a treated product selected from cultured cells; treated products such as dried cells, freeze-dried cells...; and an immobilized products of cells or treated cells" because: (1) the term "treated product" is indefinite for the reasons discussed above; (2) it is unclear whether the products recited after the term "such" are

further limiting; and (3) the term "immobilized products of cells or treated cells" is unclear. The rejection asserts that for examination purposes, the claim recites "the process according to claim 25, wherein the transformants are dried cells, freeze-dried cells, cells treated with surfactant, cells treated with an enzyme, cells treated by sonication, cells treated by mechanical milling, cells treated with a solvent, a protein fraction of a cell, or immobilized cells."

In response, claim 37 has been amended to remove the term "treated products such as" and "an immobilized products of cells or treated." Furthermore, as discussed above in regard to the term "treated product", one of ordinary skill in the art would understand after reading the instant specification especially at page 14, lines 1-6, and the examples of treated products of the culture described at page 27, lines 19-23, that the term "treated product" means treated products of the culture of the cells.

Claim 39 is said to be indefinite because the recitation "the oligonucleotide corresponding to a sequence consisting of 5 to 60 continuous nucleotides in a nucleotide sequence selected from...; or an oligonucleotide corresponding to a complementary sequence to said oligonucleotide" is unclear in regard to whether (1) the oligonucleotide comprises 5 to 60 contiguous nucleotides of the SEQ ID NO: 2; or (2) the oligonucleotide comprises a complementary sequence of SEQ ID NO: 2. The rejection asserts that for examination purposes, it will be assumed that the claim reads "an oligonucleotide selected from the group consisting of: (a) an oligonucleotide consisting of 5-60 contiguous nucleotides of the polynucleotide of SEQ ID NO: 2, and (b) the complete complement of

the oligonucleotide of (a)."

In response, Applicants have amended claim 39 as suggested by the Examiner. Therefore, the rejection of claims 15, 25-37, and 39 under 35 U.S.C. §112, second paragraph should be withdrawn.

Rejections for Written Description

Claims 15 and 25-36 are rejected under 35 U.S.C. §112, first paragraph as failing to comply with the written description requirement because the claims contain subject matter that is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed, had possession of the claimed invention. The rejection asserts that even though the specification discloses the structure of the polynucleotide of SEQ ID NO: 2 and other polynucleotides, the specification does not disclose (1) the structures of all polynucleotides which can hybridize to the polynucleotide of SEQ ID NO: 2 under any condition and encode a protein with the desired activity; (2) the structural elements in the polynucleotide of SEQ ID NO: 2 that must be present in any nucleotide to allow hybridization to SEQ ID NO: 2; and (3) the method to produce the specific compounds wherein any fraction of the culture may be used as an enzyme source. The rejection asserts that many structurally unrelated polynucleotides are encompassed by these claims. Furthermore, the specification fails to disclose a method to produce the specific compounds recited wherein

any fraction of the culture can be used as an enzyme source.

In response, Applicants note that claim 15 contains subject matter that is sufficiently described in the specification, however, solely in order to advance prosecution, claim 15 has been amended to recite an isolated DNA which codes for a polypeptide consisting of an amino acid sequence having about 99% homology with the amino acid sequence of SEQ ID NO: 1, and having an activity of producing compound (II-a) or compound (II-b) from compound (I-a) or compound (I-b). Applicants note that support for this amendment may be found throughout the specification especially at pages 9, 14-17, and Example 5. A person having ordinary skill in the art would understand, from reading the specification, that the claimed isolated DNA which codes for a polypeptide consisting of an amino acid sequence having about 99% homology with the amino acid sequence of SEQ ID NO: 1 is provided in the specification because the polynucleotide of SEQ ID NO: 41 which codes for a polypeptide consisting of the amino acid sequence of SEQ ID NO: 42 has a 99.7% homology with the amino acid sequence of SEQ ID NO: 1. As discussed throughout the specification, especially at pages 9 and 14-17, the sequence and structure of the protein having the amino acid sequence shown by SEQ ID NO: 1 is known to one of ordinary skill in the art as belonging to the genus *Bacillus*, such that the sequence and homology information may be obtained by using various gene databases.

Furthermore, Applicants respectfully submit that it is within the scope of common technical knowledge to one of ordinary skill in the art following the guidance set forth in

Applicants' disclosure, especially at pages 9, 14-17, Example 5, and SEE ID NOS: 1,2,41, and 42 that there is a high possibility that an isolated DNA which codes for a polypeptide consisting of an amino acid sequence having about 99% homology with the amino acid sequence of SEQ ID NO: 1, has an activity of producing compound (II-a) or compound (II-b) from compound (I-a) or compound (I-b).

In regard to claims 25-36, Applicants note that one of ordinary skill in the art would understand from reading the guidance set forth in the instant specification, especially at Tables 1 and 2, and Examples 1-3 and 5-6 of the instant specification, the method for producing the claimed compounds using, for example, as an enzyme source, whole cells of a microorganism which expresses a polypeptide of an amino acid sequence of SEQ ID NO: 2 and the like. Furthermore, one of ordinary skill in the art would understand after reading the specification at page 27, lines 19-23 that the "treated products of the culture" include dried cells, lyophilized cells, cells treated with surfactants, cells treated with enzymes, cells treated with ultrasonication, cells treated with mechanical milling, cells treated with solvents, protein fractions of the cells, or immobilized product of cells. It would be clear to a skilled person in the art that a polypeptide such as "protein fraction of the cells," as well as culture fractions containing the polypeptide, namely, "dried cells, lyophilized cells, cells treated with surfactants, cells treated with enzymes, cells treated with ultrasonication, cells treated with mechanical milling, cells treated with solvents, protein fractions of the cells, or immobilized product of cells," may be used as an enzyme source in the claimed

process of claims 25-36.

Therefore, the rejection of claims 15 and 25-36 under 35 U.S.C. §112, first paragraph should be withdrawn.

Rejections for Enablement

Claims 15 and 25-36 are rejected under 35 U.S.C. §112, first paragraph as failing to comply with the enablement requirement because the Examiner asserts that even though the specification is enabling for SEQ ID NO: 2 and a method for producing the specific compounds recited with the polypeptide of SEQ ID NO: 1 or a fraction of a culture containing the polypeptide of SEQ ID NO: 1, the specification does not reasonably provide enablement for: (1) polynucleotides which hybridize under any condition to the polynucleotide of SEQ ID NO: 2 and encode a protein that has the activity of producing a specific compound from another; or (2) a process for producing specific compounds as recited wherein any fraction of the culture is used as an enzyme source.

In response, and as discussed above, one of ordinary skill in the art would know that the specification enables the invention of claim 15, however, solely for the purpose of advancing prosecution of the present application, claim 15 has been amended to recite an isolated DNA which codes for a polypeptide consisting of an amino acid sequence having about 99% homology with the amino acid sequence of SEQ ID NO: 1, and having an activity of producing compound (II-a) or compound (II-b) from compound

(I-a) or compound (I-b). Applicants note that an example of DNAs which code for a polypeptide consisting of an amino acid sequence which has about 99% homology with the amino acid sequence of SEQ ID NO: 1 is provided in the specification because the polynucleotide of SEQ ID NO: 41 which codes for a polypeptide consisting of the amino acid sequence of SEQ ID NO: 42, has a 99.7% homology with the amino acid sequence of SEQ ID NO: 1. The specification provides sufficient disclosure to enable one of ordinary skill in the art to make the claimed isolated DNA which codes for a polypeptide consisting of an amino acid sequence having about 99% homology with the amino acid sequence of SEQ ID NO: 1, and having an activity of producing compound (II-a) or compound (II-b) from compound (I-a) or compound (I-b).

In regard to claims 25-36, it is commonly known to one of ordinary skill in the art, and one of ordinary skill in the art would understand, from the guidance set forth in Applicants' specification that the enzyme source may include "treated products of the culture" as described on page 27, lines 19-23. Table 1 and 2 of the present specification show that a polypeptide consisting of an amino acid sequence of SEQ ID NO: 2 has the activity of producing compound (II-a) or compound (II-b) from compound (I-a) or compound (I-b). Furthermore, the specification provides a method of using, as an enzyme source whole cells of a microorganism which expresses a polypeptide of an amino acid sequence of SEQ ID NO: 2 and the like, as shown in Examples 1-3 and 5-6. Thus, it would be clear to one of ordinary skill in the art that a polypeptide such as a "protein fraction of the cells" and culture fractions containing the polypeptide, namely,

"dried cells, lyophilized cells, cells treated with surfactants, cells treated with enzymes, cells treated with ultrasonication, cells treated with mechanical milling, cells treated with solvents, protein fractions of the cells, or immobilized product of cells," may be used as an enzyme source in the claimed process of claims 25-36.

Furthermore, Example 5 in the instant specification discloses a microorganism (*C. glutamicum* ATCC 13032 transformed with pRIyiB) which produces a polypeptide consisting of the amino acid sequence of SEQ ID NO: 42 and has an activity of converting compound (VII-a) into compound (VIII-a). One of ordinary skill in the art can readily understand from the guidance set forth in the specification, that there is a high possibility that a peptide consisting of an amino acid sequence which has about 99% homology with the amino acid sequence of SEQ ID NO: 1 has an activity of producing compound (II-a) or compound (II-b) from compound (I-a) or compound (I-b).

Therefore, Applicants' claims are enabled, and the rejection of claims 1, 2, 6, 10, 12, 14, 16, and 18 under 35 U.S.C. §112, first paragraph should be withdrawn.

Rejection Under 35 U.S.C. § 102(b)

Claim 15 is rejected under 35 U.S.C. § 102(b) as being anticipated by Rivolta et al. (Microbiology 144: 877-884, 1998). The Examiner asserts that Rivolta et al. teach a polypeptide that is 100% identical to the polypeptide of SEQ ID NO: 1, and the polynucleotide encoding that polypeptide. The polynucleotide in Rivolta et al. is asserted by the Examiner to be identical to SEQ ID NO: 2 with an exception of a

mismatch at nucleotide 462. The Examiner asserts that the polypeptide of SEQ ID NO: 1 is encoded by the of SEQ ID NO: 2 so that the polynucleotide of Rivolta encodes a polypeptide of SEQ ID NO: 1. Because claim 15 is directed to a polynucleotide that hybridizes to SEQ ID NO: 2 and encodes a polypeptide having the activity of compound II-a or compound II-b from compound I-a or compound I-b, the Examiner asserts that Rivolta teaches the claimed invention.

In response, Applicants note that Rivolta et al. is directed to a 35.7 kb DNA fragment from *B. subtilis* containing an operon that is involved in transport and degradation of extracellular carbon sources in *B. subtilis*. Although Rivolta et al. disclose the yjiB gene for *B. subtilis*, Applicants note that a nucleotide complementary to SEQ ID NO: 2 was not made nor is there direction to make this complementary nucleotide provided in the document. Furthermore, Rivolta et al. disclose only that a broad region (109° to 112°) of the chromosome DNA of *Bacillus subtilis* was determined and the predicted function of a presumed ORF. Rivolta et al. does not disclose an isolated yjiB gene. There is nothing in Rivolta et al. that teaches or suggests the claimed isolated DNA which codes for a polypeptide consisting of an amino acid sequence having about 99% homology with the amino acid sequence of SEQ ID NO: 1, and having an activity of producing compound (II-a) or compound (II-b) from compound (I-a) or compound (I-b).

Therefore, because Rivolta does not teach or suggest the Applicants' claimed invention, Applicants respectfully request that the Examiner withdraw the rejection of claim

15 under 35 U.S.C. § 102(b).

Rejection Under 35 U.S.C. § 103(a)

Claim 39 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Rivolta et al. because the document teaches an oligonucleotide that comprises the first 3 nucleotides of SEQ ID NO: 2. The Examiner asserts that Rivolta et al. does not teach a oligonucleotide consisting of 5 to 60 bases of the polynucleotide of SEQ ID NO: 2, but that it would have been obvious to one of ordinary skill in the art at the time the invention was made to make a probe 5 to 60 bases long that includes the start codon of the polynucleotide disclosed in Rivolta.

In response, and as discussed above, Applicants note that Rivolta et al. is directed to a 35.7 kb DNA fragment from *B. subtilis* containing an operon that is involved in transport and degradation of extracellular carbon sources in *B. subtilis*, and that even though Rivolta et al. disclose the yjiB gene for *B. subtilis*, Applicants note that a nucleotide complementary to SEQ ID NO: 2 was not made nor is there direction to make this complementary nucleotide provided in the document. Because there is nothing in Rivolta et al. that teach or suggest a oligonucleotide selected from a group consisting of (a) an oligonucleotide consisting of 5 to 60 continuous nucleotides of SEQ ID NO: 2, and (b) the complete complement of the oligonucleotide of (a), it would not have been obvious to one of ordinary skill in the art at the time the invention was

made to make such a probe 5 to 60 bases long just from the start codon of the polynucleotide disclosed in Rivolta et al.

For at least this reason, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claim 39 under 35 U.S.C. 103(a).

CONCLUSION

For the reasons advanced above, Applicants respectfully submit that all pending claims patentably define Applicants' invention. Allowance of the application with an early mailing date of the Notices of Allowance and Allowability is therefore respectfully requested.

Respectfully submitted,
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